

Guidance for Industry and FDA
Reviewers/Staff

**Guidance For Conducting
Stability Testing To Support An
Expiration Date Labeling Claim
For Medical Gloves**

Draft Guidance – Not for Implementation

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**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health**

**Infection Control Devices Branch
Division of Dental, Infection Control, and General Hospital Devices
Office of Device Evaluation**

Preface

Public Comment:

Comments and suggestions regarding this draft document should be submitted by [date 90 days from release date] to Chiu S. Lin, Ph.D., 9200 Corporate Blvd., Rockville, MD 20850. For question regarding the use or interpretation of this guidance contact Chiu S. Lin, Ph.D., at (301) 443-8913.

Additional Copies:

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Guidance¹ For Conducting Stability Testing To Support An Expiration Date Labeling Claim For Medical Gloves

GUIDANCE DOCUMENT

A. PURPOSE

This guidance describes the information needed to support an expiration date labeling claim for powdered or powder-free, surgeon's or patient examination gloves. Expiration dating of medical gloves is voluntary at this time. FDA recommends that manufacturers, repackagers or importers who add an expiration date labeling claim follow the recommended criteria and protocols for conducting testing described in this guidance. To ensure the visibility of the expiration date, the expiration date (month and year) should be displayed prominently on the principal display panel and/or retail packaging (i.e., the individual package), as well as on the shipping carton containing individually packaged products. The period for which the expiration date is calculated should start from the date of manufacture of the finished gloves. The claimed expiration date should be supported by data from tests demonstrating physical and mechanical integrity of the product during storage.

B. REGULATORY CONSIDERATION

Anyone intending to market a "new" medical glove in the United States with an expiration date labeling claim must follow standard regulatory procedure for introducing a new product to market. They must submit a Premarket Notification [510(k)] to FDA, and receive written notice from the FDA that the device has been found substantially equivalent to a legally marketed device before the "new" device is commercially distributed. The 510(k) should include the information described in the manual, "Medical Glove Guidance Manual." In addition, the 510(k) should include data from the testing recommended in this guidance to support the claimed expiration date. Alternately, in accordance with "A New 510(k) Paradigm-Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications", the sponsor may submit an abbreviated 510(k) that includes a summary report describing how this guidance was used to support the claimed expiration date. All records relating to a manufacturer's compliance with this guidance document must be maintained by the manufacturer for FDA inspection.

Anyone making only labeling changes to 510(k) cleared medical gloves to include an expiration date will not be required to submit a new 510(k) as long as there is no change in manufacturing processes and/or product design that affects the safety and effectiveness of the

¹ This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

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gloves. If there is a significant change in manufacturing processes and/or the product design to achieve the claimed expiration date, then the gloves would be considered a new product that requires a new 510(k).

If available, real-time aging data should be used to support the expiration date. However, if real-time data are not available, then a provisional expiration date, not to exceed a period of two years, may be established based on accelerated aging test data, as described in this guidance. FDA will allow such a provisional expiration date provided the manufacturer immediately initiates real-time stability testing to validate the proposed expiration date.

The manufacturer, importer, or repackager should compile data to support an expiration date, for a period equal to the claimed shelf-life, for each distinct glove type and model. The original testing protocols and data records based on the testing recommended in this guidance for the design and expected life of the product are to be maintained and made available during an FDA inspection. If the manufacturer, importer, or repackager can document that the shelf-life data from a previously tested product is also applicable to a new, non-tested variation of the product, then the manufacturer may apply the previously established expiration date to the new product. This documentation must be made available to the FDA upon request or during an inspection.

C. CRITERIA FOR ASSESSING CONFORMANCE

All marketed gloves must meet the glove characteristics and specifications that are presented in the 510(k). Both accelerated and real-time aged gloves are expected to meet the acceptable quality requirements (usually from ASTM standards) for barrier and physical properties testing.

The sponsor will collect samples from various lots of gloves to perform testing in accordance with statistically valid sampling plans (the FDA sampling plan for water leak testing of gloves is described in 21 CFR 800.20). It is recommended that each relevant test consist of samples that are gathered from a minimum of three separate lots. The individual lots selected should be manufactured at different times, or on different production lines or from different latex compounding lots, etc. Sample sizes must be sufficiently large enough to allow a statistically valid interpretation of the test results. The following tests are recommended:

1. Barrier: The FDA 1000 mL Water Leak Test, or ASTM D-5151.
2. Physical Properties Testing: Appropriate physical properties testing of the final finished products per ASTM D-3577, ASTM D-3578, ASTM D-5250, or an equivalent standard.
3. Packaging Integrity: Product package integrity testing or certification for sterile gloves. Testing should be documented and validated. Package integrity testing should consist of evaluating the product packaging for tensile, tear and seal strength and the puncture or impact resistance of the product packaging
4. Sterility: Documentation of product performance and conformance to specifications after sterilization if the device, manufacturing process or sterilization have been significantly changed to meet the expiration claim.

5. Other Claims: Tests to support any other claims, such as resistance to specific chemicals during the shelf-life of the glove. (Such tests are repeated at each test interval during the study.)

D. SELECTION OF STABILITY TEST PROTOCOL

The stability testing protocols should include tests commonly used by industry to demonstrate that the barrier properties, physical properties, packaging integrity, sterility and claimed attributes (special labeling claims) of the gloves are maintained for the duration of the claimed shelf-life (expiration date).

Attached to this guidance document are the FDA's recommended test protocols for accelerated aging and real-time testing entitled, "Recommended Accelerated Aging Protocol to Determine Provisional Shelf Life of Natural Rubber Latex Medical Gloves" and "Recommended Protocol for Real-Time Aging of Medical Gloves to Determine Shelf Life". For specific instructions for natural rubber latex gloves, refer to the attached "Recommended Accelerated Aging Protocol to Determine Provisional Shelf Life of Natural Rubber Latex Medical Gloves." For gloves made of synthetic materials, see further instructions at the end of this guidance.

If the manufacturer/sponsor uses a protocol, other than the ones attached, the protocol should be clearly described and documented. Manufacturers are advised to maintain the originals of all protocols, test reports, product samples, identification of persons/labs performing the test, etc., at their manufacturing establishment so that the information is available during an FDA inspection. Both accelerated and real-time stability studies should include the following information:

- a. environmental and/or storage conditions such as temperature and humidity throughout the test and storage periods,
- b. description of product packaging (e.g., individually packaged, standard sterile packaging),
- c. sample size (statistically valid sample size),
- d. test interval (e. g., every six months for the planned duration of the real-time study),
- e. test methods (identify standard method or in-house testing procedure),
- f. criteria delineating when the sample has passed or failed the test
- g. criteria delineating when the study has demonstrated or failed to demonstrate the expected shelf life,
- h. stability data,
- i. data analysis, and
- j. conclusion, proposed expiration period.

Upon successful completion of the accelerated aging testing, in addition to the gloves passing the recommended barrier, physical and mechanical properties, package integrity, and other pertinent tests, the gloves are presumed stable for up to two years pending verification through real-time testing.

E. STABILITY TESTING FOR GLOVES MADE FROM SYNTHETIC MATERIALS.

In the absence of published literature, or a national or international voluntary standard that directly address methods for establishing the shelf-life of medical gloves made from a particular synthetic material, manufacturers should develop an accelerated aging model which could be used for establishing a provisional expiration date for gloves manufactured from synthetic material. The result must be verified by real-time stability testing. The manufacturer should provide a proposed accelerated aging model, a description of the accelerated aging protocol, references to technical literature that describe the use of the accelerated aging model and how that model accounts for the pertinent degradation mechanisms specific to that material (e.g., oxidation, hydrolysis, ozonation, photo-oxidation, etc.), along with test data to support the proposed shelf-life. Manufacturers of medical gloves that are made from a combination of materials (e.g., 50% polymer A and 50% polymer B; or 40% polymer A, 30% polymer B, and 30% polymer C; where either polymer A, polymer B, or polymer C may or may not be natural rubber latex), should follow the aging protocols for the component most susceptible to degradation.

Accumulated real-time stability testing data from the beginning of the real-time study (for example, baseline data plus six-month data) should be submitted with the accelerated aging data to help verify the proposed expiration date. The labeling claims and support data will be reviewed by FDA on a case by case basis.

Recommended Protocol for Real-Time Aging of Medical Gloves to Determine Shelf Life

1. Purpose

1.1 The purpose of this document is to set forth a recommended real-time aging protocol for determining shelf life of medical gloves.

2. Normative References

2.1 The current versions of the following national consensus standards are hereby incorporated by reference:

ASTM D 573 Test Method for Rubber—Deterioration in an Air Oven,
ASTM D 3577 Standard Specification for Rubber Surgical Gloves,
ASTM D 3578 Standard Specification for Rubber Examination Gloves,
ASTM D 5151 Test Method for Detection of Holes in Medical Gloves,
ASTM D 5250 Standard Specification for Poly(vinyl chloride) Gloves for Medical Application,
and all other references incorporated therein.

2.2 The current versions of the following international consensus standards are hereby incorporated by reference:

ISO 37 Rubber, vulcanized or thermoplastic—Determination of tensile stress-strain properties,
ISO 188 Rubber, vulcanized—Accelerated ageing or heat-resistance tests,
ISO 2859 Sampling procedures for inspection by attributes,
ISO 10282 Single-use sterile surgical rubber gloves—Specification,
ISO 11193 Single-use rubber examination gloves—Specification,
and all other references incorporated therein.

3. Preparation and Sampling

3.1 An appropriate number of boxes of finished product (i.e., after final packaging and, if applicable, after sterilization) should be randomly selected from each sampling lot on the day of manufacture.

3.1.1 For the purposes of this document, the "date of manufacture" will be considered to be the date the finished product was *initially* packaged. (For gloves initially packaged in bulk and later repackaged in smaller quantities, the date of manufacture will refer to the initial packaging date.)

4. Real-time aging conditions

4.1 The appropriate number of gloves should be stored (in original packaging) in an environment representative of that expected to be encountered by the product during its lifetime, i.e., the real-time aging conditions should represent those typically encountered during transportation and storage throughout the lifetime of the product.

Example: Manufacturer XYZ usually ships gloves to the US within 2 weeks of the manufacturing date. The ship takes 2 months to reach the US. Temperatures within the shipping containers reach 45 °C and 80% relative humidity (RH). Upon reaching the US, the gloves are stored in a temperature-controlled warehouse. Therefore, Manufacturer XYZ's real-time aging study begins with storage at 45 ± 5 °C and 80 ± 5 % RH for 60 days, followed by storage at 23 ± 2 °C and 50 ± 5 % RH for the duration of the study.

4.1.1 Enough gloves should be stored so that a statistically valid sample size will be available at each test interval for all of the tests described in Section 5.

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4.2 The study should begin no later than 96 hours from the date of manufacture.

4.3 Temperature and humidity of the storage environment should be monitored and recorded at least weekly.

5. Physical and mechanical properties

5.1 In order to establish a product shelf life, physical and mechanical properties should be evaluated as described below.

5.1.1 Original physical and mechanical properties should be measured within 96 hours of the start of the real-time study. These measurements will be the baseline for the naturally aging product.

5.1.2 Physical and mechanical properties of the naturally aging product should be measured in at least six-month intervals from the date of manufacture.

5.1.3 Measurement of physical and mechanical properties should be made no later than 96 hours from the end of each consecutive aging interval.

5.2 All gloves should meet the requirements for freedom from holes as set forth in the appropriate standard (AQL = 1.5 for surgical gloves and AQL = 2.5 for examination gloves). Freedom from holes should be determined according to ASTM D 5151.

5.3 "Baseline" gloves should meet the "Before Accelerated Aging" requirements for tensile strength and percent elongation as set forth in the appropriate standard. All gloves aged 6 months and greater should meet the "After Accelerated Aging" requirements for tensile strength and percent elongation as set forth in the appropriate standard. Documentation should be in accordance with said standard(s) and include:

- a. Test specimen geometry,
 - b. Location(s) on the glove from which test specimens are obtained (including justification if more than one specimen is taken from each glove),
 - c. Thickness measurements,
 - d. Identification of apparatus used to measure thickness,
 - e. Description of testing machine and specimen grips,
 - f. Strain rate, and
 - g. Test temperature and humidity,
- as well as the required measured tensile properties.

5.4 Sterile glove packaging should be tested for package integrity and the ability to maintain sterility. Documentation should include evidence that, after storage the product packaging still meets the manufacturer's specifications for package integrity.

5.5 Tests to support other claims such as resistance to chemicals should be conducted as appropriate.

6. Determination of shelf life

6.1 The product shelf life corresponds to the last aging interval for which the product has been demonstrated to meet all of the physical and mechanical integrity criteria set forth in Section 5.

6.1.1 No sterile product should be labeled with a shelf life that exceeds the guaranteed duration of sterility of the final product.

6.2 Expiration dates are to be calculated from the date of manufacture.

6.3 Expiration dates are to include the month and year of expiry. The format of the year should be four digits; the format of the month should be letters or two digits.

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6.4 All test data should be retained by the sponsor and available for FDA review and inspection for verification that the product meets the claimed shelf life (see FDA's Guidance for Conducting Stability Testing to Support an Expiration Date Labeling Claim for Medical Gloves).

7. Test Report

7.1 A test report should be generated to document the real-time aging of the product. Test report documentation should be consistent with Sections 5.2 and 5.3 of this protocol. *In addition*, the test report should include the following:

- a. Test methods (identify whether standard method or in-house procedure),
- b. Sample size for each test conducted,
- c. Date of manufacture,
- d. Time elapsed between date of manufacture and baseline physical/mechanical properties testing,
- e. Time elapsed between date of manufacture and physical/mechanical properties testing at each aging interval (in days),
- f. Description of storage environment(s) and duration of storage at each different condition,
- g. Weekly records of storage temperature and humidity,
- h. Description of product packaging,
- i. Raw data,
- j. Data analysis,
- k. Shelf life and conclusions.

Recommended Accelerated Aging Protocol to Determine Provisional Shelf Life of Natural Rubber Latex Medical Gloves

1. Purpose

1.1 The purpose of this document is to set forth a recommended protocol for accelerated aging of natural rubber latex medical gloves which may be used to determine a provisional shelf life in the absence of real-time data. There is no guarantee that this accelerated aging protocol will give an exact correlation with real-time service performance because the behavior of elastomers at high temperatures can be unpredictable. Real-time aging data should always be collected to verify any accelerated aging approach. While real-time data is being collected, and until a more accurate model is established, the accelerated aging model outlined in this document may be used to establish a provisional expiration date of up to 2 years from the date of manufacture.

1.2 During accelerated aging, real-time aging data should be collected in accordance with the Recommended Protocol for Real-Time Aging of Medical Gloves to Determine Shelf Life, or other suitable methods, as recommended in the Guidance for Conducting Stability Testing to Support an Expiration Date Labeling Claim for Medical Gloves.

2. Normative References

2.1 The current versions of the following national consensus standards are hereby incorporated by reference:

ASTM D 573 Test Method for Rubber—Deterioration in an Air Oven,
ASTM D 3577 Standard Specification for Rubber Surgical Gloves,
ASTM D 3578 Standard Specification for Rubber Examination Gloves,
ASTM D 5151 Test Method for Detection of Holes in Medical Gloves,
ASTM D 5250 Standard Specification for Poly(vinyl chloride) Gloves for Medical Application,
and all other references incorporated therein.

2.2 The current versions of the following international consensus standards are hereby incorporated by reference:

ISO 37 Rubber, vulcanized or thermoplastic—Determination of tensile stress-strain properties,
ISO 188 Rubber, vulcanized—Accelerated aging or heat-resistance tests,
ISO 2859 Sampling procedures for inspection by attributes,
ISO 10282 Single-use sterile surgical rubber gloves—Specification,
ISO 11193 Single-use rubber examination gloves—Specification,
and all other references incorporated therein.

3. Preparation and Sampling

3.1 An appropriate number of boxes of finished product (i.e., after final packaging and, if applicable, after sterilization) should be randomly selected from each sampling lot on the day of manufacture.

3.1.1 For the purposes of this document, the "date of manufacture" will be considered to be the date the finished product was *initially* packaged. (For gloves initially packaged in bulk and later repackaged in smaller quantities, the date of manufacture will refer to the initial packaging date.)

4. Accelerated aging conditions

4.1 A predetermined, statistically appropriate number of gloves is to be stored (preferably in unopened boxes) for 90 days at 45 ± 2 °C and ambient relative humidity. In addition, a separate predetermined, statistically appropriate number of gloves is to be stored for 7 days at 70 ± 2 °C and ambient relative humidity.

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Enough gloves should be stored so that a statistically valid sample size will be available for each test described in Section 5.

4.2 Accelerated aging should be performed in an oven of the type specified in either ASTM D 573 or ISO 188.

4.2.1 Unless a compartmental-type oven is used, the simultaneous aging of certain formulations of material should be avoided, as specified in ISO 188.

4.3 Accelerated aging should begin no later than 96 hours from the date of manufacture.

4.4 Temperature and humidity of the aging chamber should be monitored and recorded at least daily. A 24-hour continuous recorder is recommended so that power interruptions or temporary equipment malfunctions can be detected.

5. Physical and mechanical properties

5.1 For the purposes of establishing a provisional product shelf life, physical and mechanical properties should be evaluated after accelerated aging as described below.

5.1.1 As per ASTM D 573, physical and mechanical properties of oven-aged gloves should be measured no earlier than 16 hours and no later than 96 hours from the time of completion of accelerated aging. During this period, the oven-aged gloves should be conditioned at 23 ± 2 °C.

5.2 All gloves should meet the requirements for freedom from holes as set forth in the appropriate standard (AQL = 1.5 for surgical gloves and AQL = 2.5 for examination gloves). Freedom from holes should be determined according to ASTM D 5151.

5.3 All gloves should meet the "After Accelerated Aging" requirements for tensile strength and percent elongation as set forth in the appropriate standard. Documentation should be in accordance with said standard(s) and include:

- a. Test specimen geometry,
 - b. Location(s) on the glove from which test specimens are obtained (including justification if more than one specimen is taken from each glove),
 - c. Thickness measurements,
 - d. Identification of apparatus used to measure thickness,
 - e. Description of testing machine and specimen grips,
 - f. Strain rate, and
 - g. Test temperature and humidity,
- as well as the required measured tensile properties.

5.4 All glove packaging should be tested for package integrity and the ability to maintain sterility. Documentation should include evidence that, after storage the product packaging still meets the manufacturer's specifications for package integrity.

5.5 Tests to support other claims such as resistance to chemicals should be conducted as appropriate.

6. Provisional establishment of shelf life

6.1 If the product meets all of the physical and mechanical integrity criteria set forth in Section 5 after 90 days of accelerated aging at 45 ± 2 °C and ambient relative humidity, and, if the product meets all of the physical and mechanical integrity criteria set forth in Section 5 after 7 days of accelerated aging at 70 ± 2 °C and ambient relative humidity, then the product may be labeled as having an expiration date up to 2 years from the

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date of manufacture. If the product does not meet all of the required criteria after accelerated aging, then the product should be labeled with a shelf life determined by real-time testing.

6.1.1 No sterile product should be labeled with a shelf life that exceeds the guaranteed duration of sterility of the final product.

6.2 All determinations of shelf life based on accelerated aging should be validated with real-time aging data (refer to the Recommended Protocol for Real-Time Aging of Medical Gloves to Determine Shelf Life).

6.3 Expiration dates are to be calculated from the date of manufacture.

6.4 Expiration dates are to include the month and year of expiry. The format of the year should be four digits; the format of the month should be letters or two digits.

6.5 All test data should be retained by the sponsor and available for FDA review and inspection as required in the Guidance for Conducting Stability Testing to Support an Expiration Date Labeling Claim for Medical Gloves.

7. Test Report

7.1 A test report should be generated to document the accelerated aging of the product. Test report documentation should be consistent with Sections 5.2 and 5.3 of this protocol. *In addition*, the test report should include the following:

- a. Test methods (identify whether standard method or in-house procedure),
- b. Sample size for each test conducted,
- c. Date of manufacture,
- d. Time elapsed between date of manufacture and onset of oven aging,
- e. Duration of oven aging,
- f. Time elapsed between completion of oven aging and physical/mechanical properties testing,
- g. Description of aging oven,
- h. Daily records of oven temperature and humidity,
- i. Description of product packaging,
- j. Raw data,
- k. Data analysis, and
- l. Expected shelf life and conclusions.